Augmentation of the *In Vivo* Elastic Properties Measurement System to include Bulk Properties

Peter H. Rogers and Michael D. Gray
G. W. Woodruff School of Mechanical Engineering
Georgia Institute of Technology
Atlanta, GA 30332
phone: (404) 894-3235 fax: (404) 894-7790 email: peter.rogers@me.gatech.edu

Award Number: N00014-13-1-0640

LONG-TERM GOALS

The goal of this project is to develop and demonstrate a system for non-invasive *in vivo* measurement of the complex elastic moduli of cetacean head soft tissues. This system is ultimately intended to provide a portable tissue characterisation and diagnostic capability for stranded animals.

OBJECTIVES

The primary objective of this project is to develop an ultrasound-based system for non-invasive determination of *in vivo* shear and bulk properties of cetacean soft tissues, including jaw fats and brain. The ultimate goal is to field a prototype system for examinations of stranded animals. Data collected with this system is intended to provide: 1) basic knowledge of *in vivo* tissue viscoelastic properties, and 2) a potential basis for diagnostics of tissue pathologies.

APPROACH

This work builds upon the principles of ultrasonic elastography[i], wherein ultrasound is used to both generate and observe low frequency vibration in soft tissues. While current methods have been successfully applied for human subjects, they are limited to tissue depths up to 5 cm, and cannot be directly extended deeper or through bone while remaining in compliance with federally mandated safety restrictions for ultrasound[ii]. Our approach was to overcome these limitations through reconsideration of the methods by which wave motion in soft tissues is generated and measured. The measurement concept thus developed, called convergent field elastography (CFE), remotely generates forces inside soft tissues using an ultrasonic transducer that produces a tube-like intensity pattern (Fig. 1). The response to this force is primarily observable as an inwardly propagating shear wave field that grows in amplitude as it converges to the center of the force pattern. A second ultrasonic transducer monitors the tissue displacement along the ultrasound beam axis, and supports an enhanced embodiment of an ultrasonic vibrometry concept[iii] previously developed at Georgia Tech and improved and adapted for elastography under the current award.

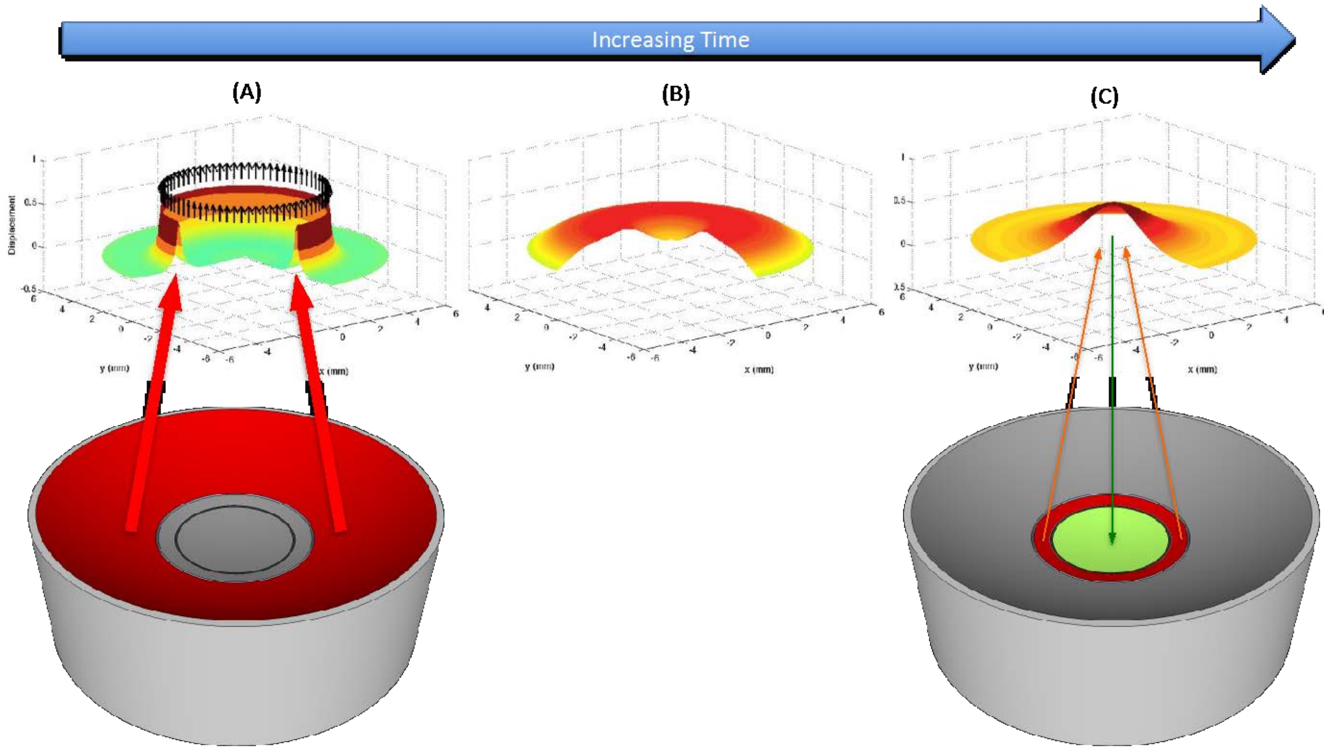

Figure 1. CFE concept. Color contour plots illustrate soft tissue displacements parallel to the transducer beam axes. (A) The annular force generation transducer transmits ultrasound (red arrows), producing a tube-like force distribution. (B) A short time after the force is applied the shear wave field converges towards the center of the force pattern. (C) The shear wave field focuses on the beam axis, producing a local maximum tissue displacement. The inner vibration measurement transducer illuminates the tissue with a low power incident signal (orange arrows) and receives backscatter (green arrow) that contains information used to determine tissue vibration along the ultrasound beam axis.

Soft tissue shear tissue properties are determined through control of the mean radius and modulation rate of the forcing field. Variation of mean radius by varying the drive carrier frequency provides information on propagation delay, which is used to estimate shear wave speed at a single frequency. By modulating (switching on and off) the forcing beam at a controlled rate, the frequency dependence of shear speed can be determined. The shear loss is subsequently found through a model fit to the observed dispersion. The unique shear field generation and detection methods, along with a lowering of ultrasonic drive frequencies, together enable CFE to image 2-3 times deeper than existing systems.

WORK COMPLETED

Ultrasonic data collected on live cetaceans was used to estimate *in vivo* ultrasonic attenuation and backscatter strength of a subset of head soft tissues[iv]. These results were used to define the properties of a homogeneous tissue phantom for use in CFE system laboratory evaluations. Shear properties were non-invasively determined at depths of 10-14 cm in the homogeneous phantom, as well as in a phantom containing small spherical inclusions with contrasting shear moduli. Additional experiments were conducted with rehydrated bottlenose dolphin and human skull samples to assess field distortion effects on CFE performance. Simulation models were developed to support all activities.

RESULTS

In vivo attenuation

Ultrasonic data collected extracranially on one *Delphinapterus leucas* and two *Tursiops truncatus* were used to estimate ultrasonic attenuation. The results shown in Figure 2 were at the low end of the range of published data, and appear to be the first of their kind for cetacean tissues.

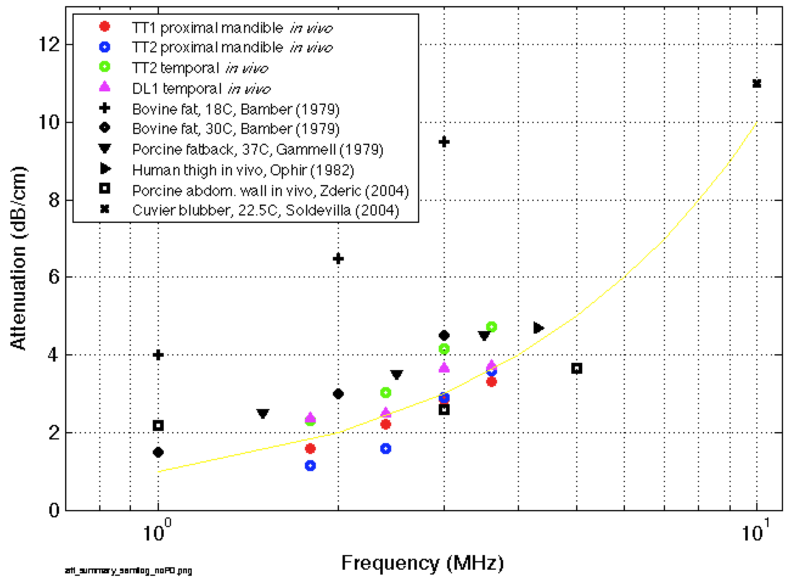

Figure 2. Ultrasonic attenuation values from the present study (color symbols) and literature (black symbols), with 1 dB/cm/MHz reference (gold line). TT: Turiops truncatus. DL: Delphapterus leucas.

Homogeneous phantom testing

The prototype CFE system was used to non-invasively determine the shear elasticity of material 10-14 cm within the homogeneous phantom built to mimic *in vivo* data. The measured time domain axial displacements shown in Figure 3 cleary indicate the ability to control forcing radius, and thereby shear wave differential delay, by changing the drive frequency. The shear elasticity, estimated from fits to displacement relative phase, was within 4.6% of the value (2.2 kPa) determined using an independent measurement made with a mechanical shaker and laser vibrometer.

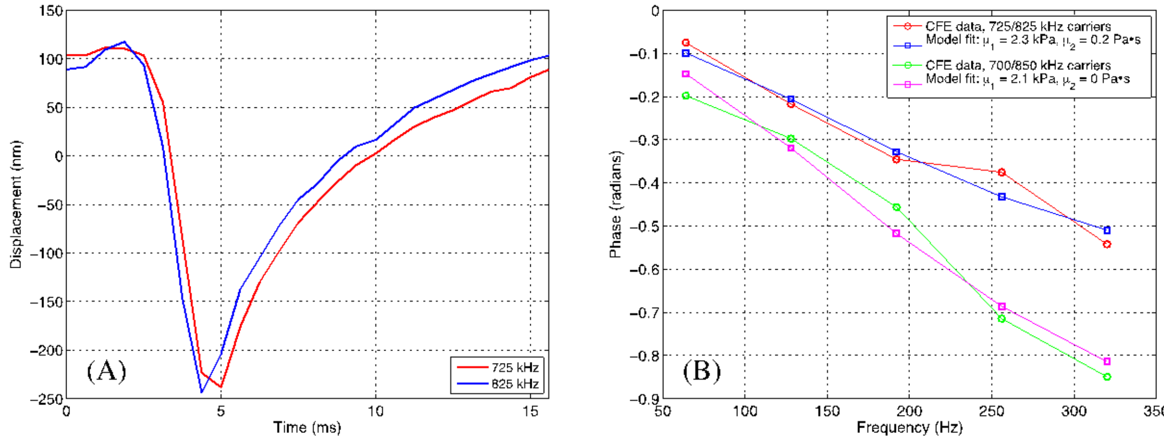

Figure 3. Examples of CFE homogeneous phantom data. (A) Time domain displacements in the focal plane, illustrating signal delay induced by force radius shift via drive carrier; (B) relative phase data and model fits for two different CFE drive carrier pairs with shear properties estimated by model fit.

Inhomogenous phantom testing

The prototype CFE system was used to image spherical shear contrast inclusions within a homogeneous "background" material, illustrated in Figure 4A. The inclusions were not visible using conventional backscatter ultrasound (Fig. 4B), but were clearly observable in images of root-mean-square ultrasound-induced displacement (4C) and estimated shear elasticity (4D). The shape of the soft inclusion was vertically truncated in the elasticity image, likely as a consequence of the axially-elongated forcing beams employed with the prototype system. The estimated elasticities of the stiff inclusion had a large variance that largely was a consequence of poor signal to noise ratio: stiffer materials yield smaller displacements and propagation delays, making the elasticity calculation more susceptible to noise. Surface waves generated at the inclusion-background interfaces probably also contributed to distortion of the elasticity images. The next iteration of the CFE system design is intended to better interpret the wave fields at the interfaces of dissimilar solids.

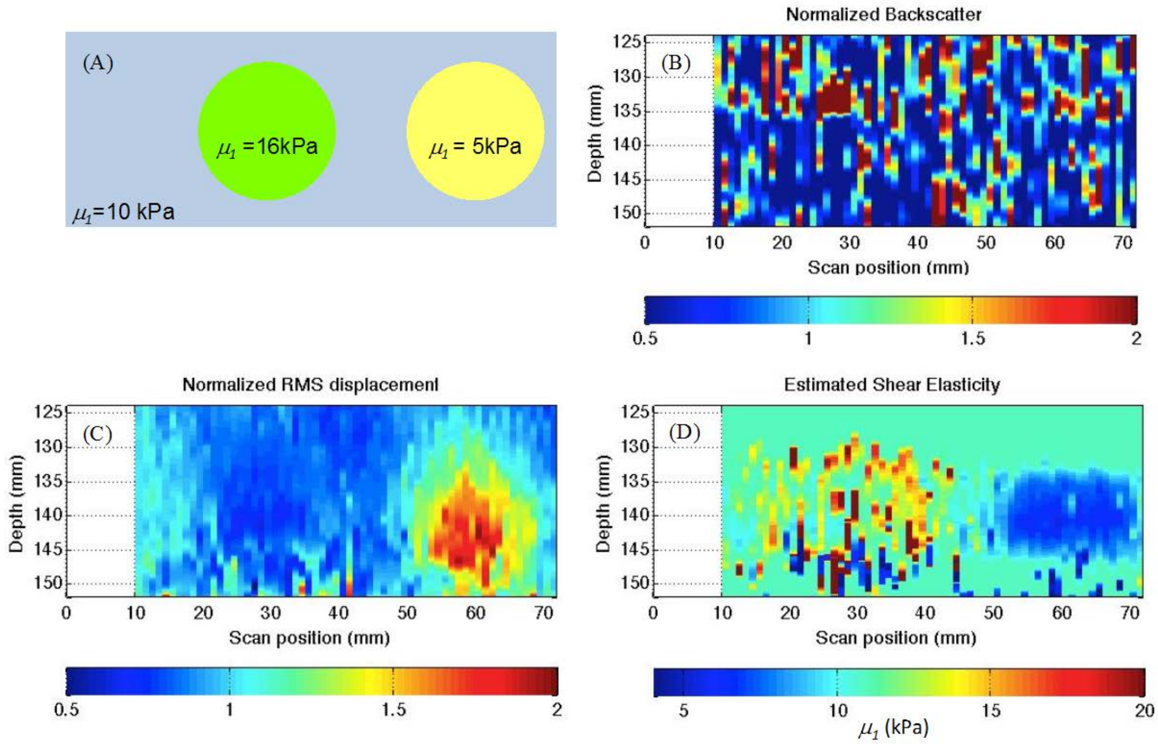

Figure 4. Inhomogeneous phantom illustration and data in a width-depth plane intersecting two spherical shear-contrast inclusions. (A) Phantom illustration with manufacturer-specified shear elasticity values; (B) normalized ultrasonic backscatter; (C) normalized RMS axial displacement; and (D) estimated shear elasticity.

Rehydrated Skull Testing

Ultrasonic pressure fields transmitted through rehydrated bottlenose dolphin and human skull samples were measured and used as inputs to a simulation in order to predict CFE performance in a homogeneous soft tissue volume obscured by bone. Figure 5 shows a summary of the predicted shear elasticities, with the symbols showing mean values by bone region, the bars showing the full range of values for the locations tested within each region, and the dashed line showing the expected elasticity value. The two regions where CFE performed best were the dolphin temporal and human parietal bones, both of which had nearly spherical concentric inner and outer radii of curvature as determined through separate ultrasonic contour mapping. Regions where CFE performance was poor were nearly flat in at least one dimension, causing significant field distortion. A phased-array implementation of the system will be needed in order to image through a broader range of bone geometries. Bone-induced attenuation and scattering quantified in this initial study also indicated that the next version of CFE would require a vibrometer digitizer with a dynamic range beyond that of the current prototype, but well within the range of commercially available electronics.

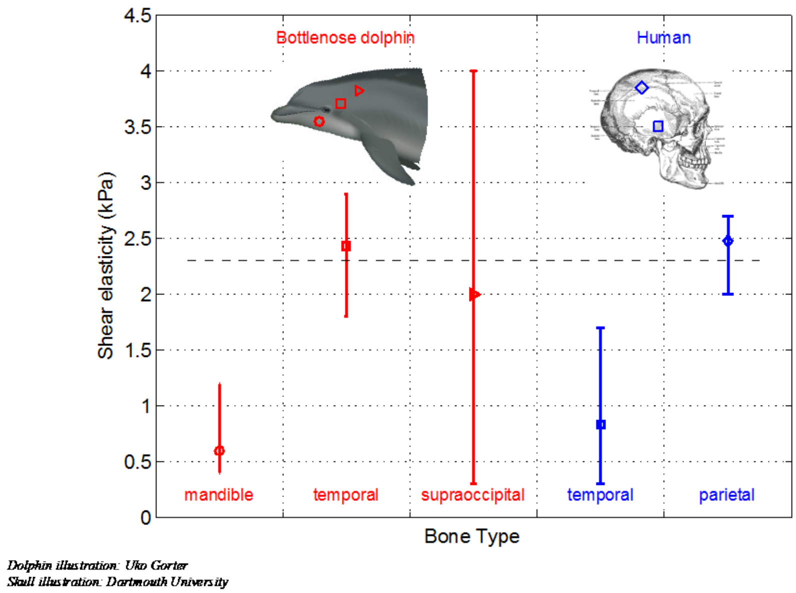

Figure 5. Simulated transcranial CFE shear elasticity estimation using measurements of field patterns transmitted through bottlenose dolphin and human skull samples.

IMPACT/APPLICATIONS

There is considerable interest in the development of structural acoustic models for the cetacean head for two main reasons: 1) to better understand biomechanics of sound reception and production in cetaceans, and 2) to understand and hopefully mitigate any harmful effects of man-made sound on their health and behavior. The development and validity of these models is severely limited by an almost complete lack of knowledge of the mechanical properties of the constituent living tissue. There is thus considerable interest in being able to measure these properties *in vivo*.

Testing to date has demonstrated the ability to measure low frequency shear properties of tissue-like materials at depths relevant to cetacean physiology studies, far beyond any capability previously demonstrated with an ultrasound-based system. A phased array version of the system, for which a preliminary design study has been completed[iv], would enable application of CFE to a broad range of non-invasive biomedical applications, potentially including those with bone in the propagation path.

REFERENCES

---

[i] Sarvazyan, A., Rudenko, O, and Nyborg, W. (2010), "Biomedical applications of radiation force of ultrasound: historical roots and physical basis", *Ultrasound in Med. & Biol.* 36(9), 1379-1394

[ii] Abbott, John G. (1999), "Rationale and derivation of MI and TI – A review", *Ultrasound in Med. & Biol.* 25, 431-441

[iii] Martin, J., Rogers, P., and Gray, M. (2011), "Range discrimination in ultrasonic vibrometry: theory and experiment", *J. Acoust. Soc. Amer. 130* (3), 1735-1747

[iv] Gray, M. (2015), "Convergent Field Elastography", Doctoral Thesis, Georgia Institute of Technology